

KOREA CONFERENCE ON ETHICAL ASPECTS OF CLINICAL RESEARCH

June 19-21, 2002
Seoul, Korea

June 18, 2002

Evening

Dinner: Speakers, Local Organizing Committee/Advisors

June 19, 2002

8:00 – 9:00 a.m.

Registration

9:00 – 10:00 a.m.

Welcome Remarks, Sang-Goo Shin, MD, PhD

Chairperson of Organizing Committee

Congratulatory Address:

1. Je Geun Chi, MD, PhD

President of the Korean Academy of Medical Sciences

2. Young-Soon Lee, DVM, PhD

Commissioner, Korean Food and Drug
Administration

Welcome Remarks, Ezekiel J. Emanuel, MD, PhD

National Institutes of Health

Introductions of Participants

10:00 – 10:45 a.m.

A Framework for the Ethics of Clinical Research

Ezekiel J. Emanuel, M.D., Ph.D.

NIH, USA

Readings:

- Emanuel E, Wendler D, Grady C. What Makes Clinical Research Ethical?
Journal of the American Medical Association 2000;283(20):2701-2711.
- Revised Declaration of Helsinki 2000.
- The Nuremberg Code
- The Belmont Report
- CFR-45: Protection of Human Subjects, DHHS, Revised June 1991.
- International Ethical Guidelines for Biomedical Research Involving Human Subjects, CIOMS Draft, Revised January 2002.
- Lederer SE. Doctors, Patients and Medical Research, pp21-23; Human Experimentation in an Age of Medical Progress, pp 132-135.

Subjected To Science, Johns Hopkins University Press, Baltimore, MD, 1995.

- Taylor T. Opening Statement of the Prosecution December 9, 1946, Chapter 5, pp 67-93, *The Nazi Doctors and the Nuremberg Code*, George Annas, Michael Grodin, eds. Oxford University Press, 1992.
- Stephens J. As Drug Testing Spreads, Profits and Lives Hang in Balance. The Body Hunters: Article I, *The Washington Post*, December 17, 2000.
- Flaherty MP, Nelson D, Stephens J. Overwhelming the Watchdogs. The Body Hunters: Article II, *The Washington Post*, December 18, 2000.
- LaFraniere S, Flaherty MP, Stephens J. The Dilemma: Submit or Suffer. The Body Hunters: Article III, *The Washington Post*, December 19, 2000.
- Pomfret J, Nelson D. In Rural China, A Genetic Mother Lode. The Body Hunters: Article IV, *The Washington Post*, December 20, 2000.
- DeYoung K, Nelson D. Latin America Is Ripe For Trials and Fraud. The Body Hunters: Article V, *The Washington Post*, December 21, 2000.
- Flaherty MP, Struck D. Life By Luck Of The Draw. The Body Hunters: Article VI, *The Washington Post*, December 22, 2000.

10:45-11:00 a.m. Break

11:00-11:15 a.m. Case about Randomization

11:15-12:30 p.m. The Ethics of Randomization and the Ethics of Placebo Controls

Jennifer Hawkins, Ph.D.
Georgetown University/University of
Toronto

Readings:

- Freedman B. Equipoise and the Ethics of Clinical Research. *New England Journal of Medicine* 1987; 317(3):141-145.
- Passamani E. Clinical Trials – Are They Ethical? *New England Journal of Medicine* 1991; 324(22):1589-1592.
- Hellman S, Hellman D. Of Mice But Not Men: Problems Of The Randomized Clinical Trial. *New England Journal of Medicine* 1991; 324(22): 1585-1589.

- Troug R. Randomized Controlled Trials: Lessons from ECMO. *Clinical Research* 1992;40(3):519-527.
- Schafer A. The Ethics of the Randomized Clinical Trial. *New England Journal of Medicine* 1982; 307(12):719-724.
- Miller F, Emanuel E. The Ethics of Placebo-Controlled Trials – A Middle Ground. *New England Journal of Medicine* 2001; 345(12):915-919.
- Freedman B. Placebo-Controlled Trials and the Logic of Clinical Purpose. *IRB* 1990;12(6):1-6.
- Beecher H. Surgery As Placebo. *Journal of the American Medical Association* 1961; 176(13):1102-1107.
- Temple R, Ellenberg S. Placebo-Controlled Trials and Active-Control Trials in the Evaluation of New Treatments: Ethical and Scientific Issues. *Annals of Internal Medicine* 2000; 133(6):455-463.
- Ellenberg S, Temple R. Placebo-Controlled Trials and Active-Control Trials in the Evaluation of New Treatments: Practical Issues and Specific Cases. *Annals of Internal Medicine* 2000; 133(6):464-470.
- Rothman J, Michels K. The Continuing Unethical Use of Placebo Controls. *New England Journal of Medicine* 1994; 331(6):394-398.
- Weijer C. Placebo-Controlled Trials in Schizophrenia: Are They Ethical? Are They Necessary?. *Schizophrenia Research* 1999;35:211-218.
- Levine R. The Use of Placebos in Randomized Clinical Trials. *IRB* 1985; 7(2):1-4.

12:30-1:30 p.m. Lunch

1:30-2:30 p.m. The Ethics of Financial Incentives for Research Participants

David Wendler, Ph.D.
NIH

Readings:

- Dickert N, Grady C. What's the Price of a Research Subject? Approaches To Payment for Research Participation. *New England Journal of Medicine* 1999; 341(3):198-203.

- Dickert N, Emanuel E, Grady C. Paying Research Subjects: An Analysis of Current Policies. *Annals of Internal Medicine* 2002;136(5):368-373.
- Wendler, D. The Ethics of Paying For Children's Participation in Research. Draft, 2002.
- McNeill, P. Paying People to Participate in Research: Why Not? *Bioethics* 1997;11(5):390-396.

2:30-2:45 p.m. Case about Recruitment and Incentives

2:45-3:30 p.m. The Ethics of Subject Recruitment
David Wendler, Ph.D.
NIH

Readings:

- pp1-31.
- Jonas H. Philosophical Reflections on Experimenting With Human Subjects. *Philosophical Reflections on Human Experimentation*
 - Council on Ethical and Judicial Affairs, AMA, Subject Selection for Clinical Trials. *IRB* 1998;20(2):12-15.
 - Weijer C. Evolving Ethical Issues in Selection of Subjects For Clinical Research. *Cambridge Quarterly* 1996;5:334-345.
 - Office of Inspector General, DHHS. Recruiting Human Subjects: Pressures In Industry-Sponsored Clinical Research; OEI-01-97-00195, June 2000.

3:30-3:45 p.m. Break

3:45-4:00 p.m. Case On Informed Consent

4:00-5:00 p.m. Individual Informed Consent
Gopal Sreenivasan, Ph.D.
NIH

Readings:

- Appelbaum P, Roth L, Lidz C, Benson P, Winslade W. False Hopes And Best Data: Consent To Research and The Therapeutic Misconception. *The Hastings Center Report* pp 20-23, April 1987.
- Levine R. Informed Consent in Research and Practice. *Archives of Internal Medicine* 1983; 143:1229-1231.
- Berg JW, et al. The Legal Requirements for Disclosure and

Consent: History and Current Status. From *Informed Consent: Legal*

Theory and Clinical Practice, 2nd Edition. pp 41-74. Oxford

University

Press, New York 2001.

- Guidelines for Writing Informed Consent Documents, OHSR, NIH.
- Recommendations for the Development of Informed Consent Documents for Cancer Clinical Trials, NCI, NIH.

5:30-7:00 p.m.

Welcome Reception (Garden View Restaurant)

June 20, 2002

9:00-9:15 a.m.

Case about Stored Biological Samples

9:15-10:00 a.m.

The Ethics of Research with Stored Biological Samples

James Lavery, Ph.D.

FIC, NIH, USA

Readings:

- Clayton EW, et al. Informed Consent for Genetic Research On Stored Tissue Samples. *Journal of the American Medical Association* 1995;274(22):1786-1792.
- National Bioethics Advisory Commission, Research Involving Human Biological Materials: Ethical Issues and Policy Guidance, Executive Summary And Chapter 1, August 1999.
- American Society of Human Genetics, ASHG Report: Statement Of Informed Consent for Genetic Research. *American Journal of Human Genetics* 1996;59:471-474.
- American Society of Human Genetics, Ad Hoc Committee on DNA Technology; DNA Banking and DNA Analysis: Points To Consider. *American Journal of Human Genetics* 1988;42:781-783.
- Merz J, Sankar P, et al. Use of Human Tissues in Research: Clarifying Clinician and Researcher Roles and Information Flows. *Journal of Investigative Medicine* 1997;45(5):252-257.
- Glass KC, Weijer C, et al. Structuring the Review of Human Genetics Protocols: Gene Localization and Identification Studies. *IRB* 1996;18(4):1-9.

- Beskow L, Burke W, Merz J, Barr P, Terry S, Penchaszadeh V, Gostin L, Gwinn M, Khoury M. Informed Consent for Population-Based Research Involving Genetics. *JAMA* 2001;286(18):2315-2321 and 1-7 (Supplemental Brochure).

10:00-10:15a.m. Case about Conflict of Interest

10:15-10:30 a.m. Break

10:30-11:15 a.m. The Ethics of Conflict of Interest
Dr. Ambrose Talisuna
Ministry of Health, Kampala, Uganda

Readings:

- Rothman K. Conflict of Interest: The New McCarthyism In Science. *Journal of the American Medical Association* 1993;269(21):2782-2784.
- Thompson D. Understanding Financial Conflicts of Interest. *New England Journal of Medicine* 1993;329(8):573-576.
- Thompson D. Ethics in Congress: From Individual to Institutional Corruption. *Corrupt Connections* The Brookings Institute 1995, Pp 124-130.
- Emanuel E, Steiner D. Institutional Conflict of Interest. *New England Journal of Medicine* 1995;332(4):262-267.
- Rodwin, MA. Physicians' Conflict of Interest: the Limitations of Disclosure. *New England Journal of Medicine* 1989;321(14):1405-1408.
- Martin JB, Kasper DL. In Whose Best Interest? Breaching the Academic-Industrial Wall. *The New England Journal of Medicine* 2000;343(22):1646-1649.
- Cho MK, Shohara R, Schissel A, Drummond R. Policies on Faculty Conflicts of Interest at US Universities. *JAMA* 2000;284(17):2203-2208.
- Korn, D. Conflicts of Interest in Biomedical Research. *JAMA* 2000;284(17):2234-2235.
- Wazana, A. Physicians and the Pharmaceutical Industry – Is a Gift Ever Just a Gift? *JAMA* 2000;283(3):373-380.
- Stelfox HT, Chua G, O'Rourke K, Detsky A. Conflict of Interest in the Debate Over Calcium-Channel Antagonists. *The New England Journal of Medicine* 1998;101-106.

- Lo B, Wolf L, Berkeley A. Conflict-Of-Interest Policies for Investigators in Clinical Trials. *The New England Journal of Medicine* 2000;343(22):1616-1620.
- McCrary S, Anderson C, Jakovljevic J, et al. A National Survey of Policies on Disclosure of Conflicts of Interest in Biomedical Research. *The New England Journal of Medicine* 2000;343(22):1621-1626.

11:15-11:30 p.m. Case About Risks of Research

11:30-12:30 p.m. The Ethics of Risk-Benefit Assessments

Reidar K. Lie, M.D., Ph.D.

University of Bergen, Norway and NIH

Readings:

- King N. Defining and Describing Benefit Appropriately In Clinical Trials. *Journal of Law, Medicine & Ethics* 2000;28:332-343.
- Meslin E. Protecting Human Subjects from Harm Through Improved Risk Judgements. *IRB* 1990;12(1):7-10.
- Directive 2001/20/EC of the European Parliament and of the Council of 4 April 2001. *Official Journal of the European Communities* 2001.
- Protocol to the Convention: Convention for the Protection of Human Rights And Dignity of the Human Being with Regard to the Application of Biology And Medicine: Convention on Human Rights and Biomedicine. Oviedo, 4.IV.1997.

12:30-2:00 p.m. Lunch

2:00 – 2:15 p.m. Case on Genetics Research

2:15-3:15 p.m. The Ethics of Genetics Research

Benjamin Wilfond, M.D.

NIH

Readings:

- Geller G, Botkin J, Green M, Press N... et al. Genetic Testing for Susceptibility to Adult-Onset Cancer. *JAMA* 1997;277(18):1467-1474.
- Juengst, ET. Human Genetics '98: Ethical Issues in Genetics – Group Identify and Human Diversity: Keeping Biology Straight from Culture. *American Journal of Human Genetics* 1998;63:673-677.

- Botkin JR, McMahon WM, Smith KR, Nash, JE. Privacy and Confidentiality in the Publication of Pedigrees. *JAMA* 1998;279(22):1808-1812.
- Botkin, JR. Protecting the Privacy of Family Members in Survey and Pedigree Research. *JAMA* 2001;285(2):207-211.
- Byers PH, Ashkenas J. Human Genetics '98: Ethical Issues in Genetics – Pedigrees-Publish? Or Perish the Thought? *American Journal of Human Genetics* 1998;63:678-681.

3:15-3:30 p.m. Break

3:30-4:15 p.m. Function and Performance of Ethical Review
Vichai Chokevivat, MD, MPH
FDA, Thailand

Readings:

- Freedman B, Fuks A, Weijer C. Demarcating Research and Treatment: A Systematic Approach for the Analysis of the Ethics of Clinical Research. *Clinical Research* 1992;40: 653-660.
- Operational Guidelines for Ethics Committees That Review Biomedical Research, WHO, Geneva 2000.
- Lemmens T and Freedman B. Ethics Review for Sale: Conflict of Interest and Commercial Research Review Boards. *The Milbank Quarterly*, 2000; 73:547-584.
- Levine, RJ. The Institutional Review Board, Chapter 14 from *Ethics and Regulation of Clinical Research, Second Edition* Yale University Press, New Haven 1988:321-363.

4:15-5:30 p.m. Mock IRB

Reidar K. Lie, M.D., Ph.D.
University of Bergen, Norway and NIH

7:00 p.m. Dinner - Informal

June 21, 2002

9:00-10:30 a.m. Stem Cell Research
John Harris, Ph.D.
Manchester University, United Kingdom

Readings:

- NBAC. Executive Summary: Ethical Issues in Human Stem Cell Research. September 1999. Rockville, Maryland.

- UK Department of Health. Government Response to the Recommendations Made in the Chief Medical Officer's Expert Group Report "Stem Cell Research: Medical Progress with Responsibility." August, 2000.
- Harris, J. The ethical use of human embryonic stem cells in research and therapy. A Companion to Genethics: philosophy and the genetic revolution. Justine C. Burley and John Harris Eds. Basil Blackwell, Oxford. 2001.
- Opinion of the European Group on Ethics in Science and New Technologies to the European Commission. Ethical Aspects of Human Stem Cell Research and Use. No. 15. November 14, 2000.
- UK Department of Health. Stem Cell Research: Medical Progress with Responsibility. Report from the Chief Medical Officer's Expert Group. June, 2000.
- Lanza R, Caplan A, Silver M... et al. The Ethical Validity of Using Nuclear Transfer in Human Transplantation. *JAMA* 2000; 284(24):3175-3179.
- Juengst E, Fossel M. The Ethics of Embryonic Stem Cells – Now and Forever, Cells Without End. *JAMA* 2000; 284(24):3180-3184
- Cohen C, Dresser R, Lanza R, et al, Juengst E, Fossel M. Letters: Ethical Issues in Embryonic Stem Cell Research. *JAMA* 2001; 285(11): 1439-1440.
- Weissman, IL. Stem Cells-Scientific, Medical, and Political Issues. *New England Journal of Medicine* 2002; 346(20): 1576-1579.
- Annas, GJ. Cloning and the U.S. Congress. *New England Journal of Medicine* 2002; 346(20): 1599-1602.
- Outka, G. The Ethics of Stem Cell Research. Unpublished Manuscript. 2002.

10:30-10:45 a.m. Break

10:45-12:00 pm A Framework for Evaluating International Collaborative Research

Ezekiel J. Emanuel, M.D., Ph.D.
NIH, USA

Readings:

- Emanuel E, Wendler D, Killen J, Grady C. What Makes Multi-National Research Ethical? (manuscript)
- Beyond Reasonable Availability: An Ethical Framework for Determining Benefits of Research in Developing Countries. (Manuscript)

- Glantz L, Annas G, et al. Research in Developing Countries: Taking "Benefit" Seriously. *The Hastings Center Report* 1998;28(6):38-42.
- Shapiro HT, Meslin EM. Ethical Issues In the Design and Conduct of Clinical Trials in Developing Countries. *New England Journal of Medicine* 2001;345:139-142.
- International Ethical Guidelines for Biomedical Research Involving Human Subjects, CIOMS Draft, Revised January 2002.
- Phanuphak, P. Ethical Issues in Studies in Thailand of the Vertical Transmission of HIV. *The New England Journal of Medicine* 1998;338(12):834-835.
- Lurie P, Wolfe S. Unethical Trials of Interventions to Reduce Perinatal Transmission of the Human Immunodeficiency Virus in Developing Countries. *The New England Journal of Medicine* 1997;337(12):853-856.
- Angell, M. Investigators' Responsibilities for Human Subjects in Developing Countries. *New England Journal of Medicine* 2000;342(13):967-969.
- Angell, M. The Ethics of Clinical Research in the Third World. *New England Journal of Medicine* 1997;337(12):847-849.
- Bloom, B. The Highest Attainable Standard: Ethical Issues in AIDS Vaccines. *Science* 1998;279:186-188.
- Crouch R, Arras J. AZT Trials and Tribulations. *The Hastings Center Report* 1998;28(6):26-34.
- Grady, C. Science in the Service of Healing. *The Hastings Center Report* 1998;28(6):34-38.
- Macklin, R. After Helsinki: Unresolved Issues in International Research. *Kennedy Institute of Ethics Journal* 2001;11(1):17-36.
- Nuffield Council on Bioethics. The Ethics of Research Related to Healthcare in Developing Countries, 2002. Ch. 7: Standards of Care, 87-97. Ch. 9: What Happens Once Research Is Over?, 113-126.

12:00-1:30 p.m.

Lunch

1:30-3:30 pm

Discussion of Regulation of Stem Cell Research in Korea
Regine Kollek , Ph.D. - Moderator
University of Hamburg and
German National Ethics Council, and

Ezekiel Emanuel, M.D., Ph.D
NIH, USA

Shin-Yong Moon, MD, PhD
Seoul National University

3:30 pm

Wrap-up & Closing Remarks

Ezekiel Emanuel, M.D., Ph.D
NIH, USA

Sang-Goo Shin, MD, PhD
Chairperson of Organizing Committee